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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,289	04/20/2001	David B. Fick	370143-66	3676

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EXAMINER
PATEL, SUDHAKER B

ART UNIT	PAPER NUMBER
1624	5

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/839,289	David B. Fick et al
Examiner	**Art Unit**
Sudhaker Patel	1624

-- Th MAILING DATE of this communication app ars on the cov r sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Jan 29, 2002

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-35 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☒ Claim(s) 34 and 35 is/are allowed.

6) ☒ Claim(s) 1-33 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims(in part)1-35, drawn to compounds, compositions and a method of use for bioavailability properties for the generic Formula A}-L-CO-{B wherein A is a 9-atom bicyclic moiety in which the five membered ring has 1 Nitrogen N1 and A2, A3 = Carbons, classified in class 514, subclasses 254.09, 678.

II. Claims(in part) 1-35, drawn to other compounds not included in Group I where in A = 9-atom bicyclic moiety in which A2, A3 = N i.e. Part of the fused ring forms triazole core, classified in class 548, subclasses various depending on the nature of the variables R2,R3,R5,R5',R6, R6' R7 etc. If this group is elected further restriction/election will be required as there are many unknowns.

Applicants are required to elect one of the above inventions together with a single species encompassing the elected invention in replying to this Office Action.

2. The inventions are distinct, each from the other because of the following reasons: Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the

instant case 4H-Indol-4-0ne, 1,5,6,7-tetrahydro-1-(2-hydroxyethyl)- (= CAS RN 186963-73-5) which a N-substituted 9-atom bicyclic moiety can be used in formulating "Oxidative hair dye compositions as shown in ref. EP 780118".

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. This application contains claims directed to the following patentably distinct species of the claimed invention: Together with different values for components A2/A3, the other variables R2, R3, R5, R5', R6, R6' will provide many compounds which are non-equivalent to each other..

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 1,34,35 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable

thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. During a telephone conversation with Mr. M. B. Farber on 3/4/02 a provisional election was made with traverse to prosecute the invention of Group I, claims(in part)1-35 wherein the generic Formula of claim 1 has a 9-membered bicyclic moiety with A2/A3 = Carbons. Since claims 1-35 link with other invention, applicants are urged to limit the scope of the same to elected invention, and delete non-elected subject matter. Therefore, the instant application will be examined bearing in mind the subject matter of invention of Group I as elected by the applicants only. Affirmation of this election must be made by applicants in replying to this Office action, and after rechecking the claim dependency.

8. Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Drawings

9. The subject matter of this application admits of illustration by a drawing to facilitate understanding of the invention. Applicant is required to furnish a drawing under 37 CFR 1.81. No new matter may be introduced in the required drawing.

Notice of Draftperson's Patent Drawing Review is herewith enclosed.

Claim Rejections - 35 U.S.C. § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any

person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.\

A). The claims language recite "A tetrahydroindolonone derivative". It is suggested to correct the same as:"The compound of Formula".

B).The generic claim 1 has (ii). A2 and A3 defined under (A) to (F). If these are provisos to avoid prior art(s) applicants are urged to provide necessary copies of the documents and their relevancy to instant application because it will be necessary for the examination of the current case.

C).Claim language recites" analogue". It is not very clear as to what applicants want to include under this term. Clarification is requested.

D). Claim 16 recites " to increase the bioavailability properties....". Applicants' intentions are not very clear. Does it mean that the compounds can be further oxidized by air oxidation or oxygen of water? Clarification is requested.

E). Claim 33 recites " a logP of from about 1 to about 4". It is not very clear as to what applicants want to accomplish. Is it pH of the compound which must be acidic? Clarification is requested.

Claim Rejections - 35 U.S.C. § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-33 are rejected under 35 U.S.C. 112, para one because the specification, while enabling as a method of making/using a composition consisting of species of claim 34,35 for the compounds of the invention of Group I, does not reasonably provide enablement for other compounds or their compositions, or derivatives encompassing moiety B as represented having a variety of moieties, including moieties having nootropic activity or other biological or physiological activity involving "bioavailability properties & having a logP of about 1 to about 4" as recited in claim 16 and claim 33 respectively.

SCOPE OF ENABLEMENT:

In cases directed to chemical compounds which are being used for their physiological/biological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See in re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group and In re Wiggins 179 USPQ 421.(2). Pharmaceutically acceptable moieties having at least one polar, charged, or hydrogen-bond forming group to increase the bioavailability properties of the tetrahydroindolone derivatives or analogue" as recited in the claims reads on all such moieties regardless of complexity of structure and point of attachment to the heterocyclic core for which there is no sufficient teaching how to make and how to use at any one selective location among the many possible sites present. The situation is more confusing when a skilled person in the art tries to visualize the multiple possibilities of claims 1(or claims dependent on it) and/ or its composition or its analogue/derivative form. Applicants provide no reasonable assurance that any and all analogues

of the instant compounds and their derivatives as outlined above, will have ability to increase the bioavailability properties by one or more processes/method(s).

In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include:*(1).* The nature of invention;*(2).* the state of prior art ;*(3).* the predictability or lack thereof in the art; *(4).* the amount of direction or guidance present;*(5).* the presence or absence of working examples;*(6).* the breadth of the claims, and *(7).* the quantity of experimentation needed.

Applicants' attention is also drawn to fact that the development path for a laboratory compound to medicine as a " compound, derivative or analogue" is an accepted very difficult and complicated process, and the reader(examiner) is left to visualize the merits of the animal model testing to be converted into a utility for mammals including humans without actually testing on human. Together with this when one considers the toxicity/tolerance/efficacy/effectiveness aspect for human, it is very confusing to read the same from the claims as they are presented. Particular attention is called to Ex parte Busse 1 USPQ 2nd 1908, which had testing no less impressive than

here, and on a claim with just a single species. Yet the claim was refused.

Claims 1-33 are rejected, 35 U.S.C. 112 para. 1 and 35 U.S.C. 101 as lacking enablement for the alleged utility " to increase the bioavailability properties".

The quantity of experimentation need would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skilled in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims involving use of compounds, their compositions.

Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a single compound for a method of increasing the bioavailability properties as claimed herein.. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech v.s. Novo Nordisk*, 42 USPQ 2nd.

One skilled in the art would not accept the utility as obviously valid and correct. In re Citron,(CCPA 1964) 325 F2d 248, 139 USPQ 516; In re Hartop et al. (CCPA 1962) 311 F2d 135 USPQ 419.

Allowable Subject Matter

Compound claims 2-33, 34,35 will be considered for allowance, provided applicants attend the various issues as mentioned above, and also limit the scope of the claims to subject matter as elected.

Conclusion

12. The following is a statement of reasons for the indication of allowable subject matter:

The closest prior art ref. Terranova et al (EP 754681) recites the compounds having CAS RN 186963-75-7 (= 4H-indol-4-one,1-(2,3-dihydroxypropyl)-1,5,6,7,-tetrahydro-) i.e. N-substituted by propyl moiety. The ref.,. Differ from the instant compounds by not having substituted propionic acid derivatives, and additionally there is not suggestion or indication by the ref. to arrive at the instant compounds having pharmacological activity by way of motivation.

This application has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is, therefore, requested in promptly correcting any errors of which they may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker Patel,D.Sc.Tech. whose telephone number is (703) 308 4709.

The examiner can normally be reached on Monday thru' Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Dr.Mukund Shah can be reached at (703) 308 4716.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

Any inquiry of general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308 1235.

Mukund J. Shah

SUPERVISORY PATENT EXAMINER

Group 1600

S.p.

March 5, 2001.